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Uchtenhagen, Ambros

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The role and function of heroin-assisted treatment at the treatment system level

Ambros Uchtenhagen

Swiss Research Institute for Public Health and Addiction at Zurich University

Summary

Introduction: Prescribing opium, morphine and heroin to opiate addicts has a long history, as an approach to prevent negative consequences from excessive and uncontrolled use. It rarely reached the majority of this target population. During the 20th century, moral concerns mainly led to control measures and total prohibition (except for medicinal use and research). Other opioid agonists replaced opiates for maintenance therapy; Methadone and Buprenorphine maintenance became the preferred approaches to reach out effectively heroin addicts and to allow for significant improvements in health and social status of patients. Their role for the treatment system is essential. **Aim:** to describe the revival, role and function of heroin-assisted treatment (HAT), and to review critical concerns against this approach in the light of research evidence. **Methods:** research reports, reviews and monographs on opiates, agonist maintenance treatment and HAT. **Results:** The extent of HAT in countries where it is available is modest, in comparison to other agonist maintenance treatments for opiate dependence. Within the European Union, the role of HAT is marginal. A range of therapeutic, safety, prevention and economic concerns about potential negative effects of HAT, for patients and for the treatment system, are discussed in the light of relevant research evidence. None of the concerns is justified. Positive effects for the treatment system and for public order prevail. **Conclusions:** the present model of HAT has good outcomes for previously treatment-resistent heroin addicts, is a safe and cost-effective therapy and a useful element in a comprehensive treatment system for heroin addicts.

Key Words: Opioid maintenance; heroin-assisted treatment; treatment system

1. Introduction: opiates for opiate addicts

The idea and the practice of providing opiates to people dependent on opiates are not new. The widespread use of opium as an analgesic leading to what we term a dependence syndrome in chronic patients dates back to antiquity, and examples of maintenance regimes became known early in the 20th century [32]. Following the extraction of morphine and the invention of hypodermic injections, opiate analgesia became more effective and widely used, the incidence of the dependence syndrome rose, and led to the practice of prescribing morphine to those who were dependent. When heroin (diacetylmorphine) was discovered, it not only found use as a replacement for morphine; it became a component in so-called patent medicines that were prescribed in great quantities. This resulted in its extended use and first observations of heroin dependence – and again in regimes that are based on prescribing the substance for treatment and maintenance [4, 18, 23, 27, 31].

The reaction against any use of heroin was not so much based on scientific data about the shortcomings or negative effects of such use. It mainly came from moralistic concerns that demonized heroin as a threat to society and heroin addicts as criminals. The result was a stepwise process of control measures [20, 26]. This process finally led to prohibition worldwide, as stated in the UN Single Convention on Narcotic Drugs [34]. In 9 countries only, heroin was still legally prescribed as medicine [16], and its prescription to heroin addicts became a British specialty [16, 26].

Other forms of agonist maintenance treatment of opiate dependence started in Canada and USA with the prescription of oral methadone. Later on, a diversification took place, with the use of buprenorphine, codeine and morphine as orally applicable opioid medications for illegal opiates, and the practice of

Corresponding author: Ambros Uchtenhagen, Swiss Research Institute for Public Health and Addiction at Zurich University, Konradstr. 32, CH-8029 Zurich, Switzerland.
E-mail: uchtenhagen@isgf.uzh.ch

writing out prescriptions to addicts was replaced by more comprehensive care programmes. This model became the most cost-effective treatment for opioid dependence, and was recommended as forming the "backbone of the treatment system for opioid dependence" [37]. However, an ideological debate on maintenance treatment as an ethically unacceptable tool continued, and the dispute between abstinence-only and agonist maintenance therapies gave way only recently to an integrative concept of opioid dependence treatment [33].

2. The role of opioid maintenance therapy at the system level

Reliable data on the proportion of opiate addicts covered by maintenance regimes in history are rare. Apparently, even in countries with traditional availability of opium, such regimes were not widespread (for South-east Asia see [35], for England see [2]). Narcotic clinics in the USA attracted a small percentage of the rapidly increasing addict population [19]. In contrast, the percentage of heroin addicts covered by prescribing practitioners and specialized clinics in England was probably rather high; according to Home Office data, 1,288 out of 1,418 registered narcotic addicts were in outpatient treatment by the end of 1972, and it is reasonable to presume that a large majority of outpatient treatment consisted in maintenance regimes [16]. In recent years, a high proportion of coverage is documented in some member states of the European Union by agonist maintenance treatments, mainly using methadone and/or buprenorphine. Coverage throughout the Union was ca. 700,000 out of 1.3 million heroin addicts by 2009 [6].

3. A revival of heroin prescription for maintenance

Why should heroin be taken up again as a medication in maintenance treatment? Two reasons must be mentioned here: first, the advent of the HIV epidemic among injecting addicts raised serious public health concerns; the intimate partners of injectors are at high risk of becoming infected and thereby a threat to the population at large. Second, the growing numbers of heroin addicts for whom other agonist maintenance treatments failed increased with the total numbers enrolled in such maintenance, and there was need for an attractive alternative.

Lastly, a competitive and aggressive heroin market as well as a rapidly increasing number of marginalized heroin injectors, culminated in large open drug scenes in major cities and resulted in creating an unacceptable public nuisance. This highly visible indicator of an inefficient drug policy called for a new orientation. In 1991, the Swiss Federal Government issued a new drug policy, which included harm reduction measures, as well as innovative approaches in prevention, treatment and law enforcement. One of the innovations was a national research project on HAT, based on a new model of supervised heroin injecting in the framework of a comprehensive assessment and therapeutic programme.

4. The Swiss model of HAT: learning from history

When preparing the Swiss national study, former experiences with this approach had to be considered. British heroin prescribing had adapted considerably to the changed characteristics of patients, among whom there were by then many young marginal injectors instead of socially integrated pain patients with iatrogenic heroin dependence. The adaptation consisted in mailing prescriptions directly to pharmacies instead of handing them out to patients, regular consultations, urine control, dosing restrictions. Central registration made it difficult to get prescriptions from multiple doctors. "The structural transformations brought about by the clinics have enabled the growth of the therapeutic essential – a relationship between doctor and addict in which both must expect that they will be working together over months and years" [16]. The obligation to notify patients receiving heroin for a central registry was suspended in 1997 [18].

The narcotic clinics in the southern states of the USA with rather socially integrated patients and well structured programmes were effective, whereas clinics in urban areas in the North suffered from problems with large numbers of illegal injectors involved in criminal activities [19].

When the Swiss Federal Government agreed to start a scientific project with heroin-assisted treatment, this had to reach out to the disintegrated young injectors in the large open drug scenes in urban areas. The justification came from public health and public order concerns. Positive results were not only expected for the benefit of addicts; the main objective was to improve an intolerable situation aiming at effects at population level. The Federal Drug Commission received the mandate to prepare such a project, and one of the first steps taken was to ask Dr. Mino to write a

review of all former experiences with heroin and morphine prescribing. In her report, she concluded with a number of recommendations drawn from her previous experience. She firmly recommended criteria providing indications based on the given epidemiological and therapeutic situation, a defined indication process and intake procedure, prescribing heroin in public clinics only, with small-scale experiments to be evaluated after 2 years [19].

On the basis of her recommendations, the research protocol for the Swiss cohort study was set up, discussed and approved in the Federal Narcotic Commission, the National Health Authorities, and lastly at Federal Government level. This process resulted in the following main characteristics of the project [34]:

Restrictive indication criteria (only for chronic opiate-dependent patients for whom other treatments had failed repeatedly, and who are suffering from health and/or social deficits, minimal age (20 years), minimal documented duration of heroin dependence (2 years);

- Centralized intake procedure (at Federal Office of Public Health);
- Centrally authorized outpatient clinics only with multi-disciplinary teams;
- Supervision and continued education of teams;
- The framework of a comprehensive assessment and therapeutic programme;
- A needs-based individual regime;
- The strictly supervised intake of injectable opiates;
- Driving of motor vehicles not permitted;
- Exclusion of simultaneous enrollment in another heroin substitution programme;
- Consent of patients and staff to providing all the data and examinations required for the evaluation process.

An independent international expert group of experts, nominated by WHO, controlled the implementation, and commented on the evaluation report, suggesting more randomized controlled studies [1]. Following their recommendations, the Swiss model of HAT was subsequently used in the Netherlands, Germany, Spain, Canada and England, in randomized controlled trials. The characteristics and the positive outcomes of all trials have been published in great detail [28, 29]. Significant improvements in health and social integration, which were superior in experimental groups compared with control groups, made HAT an interesting additional approach for treatment-refractory heroin addicts. How well is it accepted as part of the treatment system?

5. Extent of HAT at the treatment system level

First, we should look at the extent of traditional heroin prescribing in the UK. A 1995 survey of drug services commented on the current practice of heroin prescription. The Home Office recorded 55 current heroin licenses. The majority of doctors wrote prescriptions for only a few patients. The total number of patients was 323 [8]. A survey published in 2001 showed that, of 70 doctors who had a licence for prescribing heroin, only 47 made use of it. The licence is available through the Home Office and only for specialized psychiatrists working in public clinics; it is valid for 3 years. The obligation to enroll patients receiving heroin in a central registry was suspended in 1997. Existing guidelines for heroin maintenance no longer supply details. There are no defined indication criteria. However, as a rule, patients had tried other treatments previously and documented an extended career of heroin dependence [18, 27].

What is the present situation in countries where trials with supervised injected heroin took place, and at the European level?

HAT is provided as a regular treatment for otherwise treatment-refractory heroin addicts in Denmark, Germany, the Netherlands and Switzerland. In these countries, HAT clinics are part of the regular treatment system. In Spain and Canada, patients formerly involved in trials in their respective countries may continue to receive HAT, but no new patients are being admitted. The future of the English clinics depends on local funding after the end of national funding. Up to now, Denmark is the only country starting HAT as a regular treatment without previously conducting a research project (in view of the evidence coming from trials in other countries).

The capacity of HAT is minimal, at best modest when compared with the total capacity of agonist maintenance treatment for opioid dependence (Table 1). Based on the currently available information, HAT is provided in 58 clinics located in 8 countries, but to less than 1% of all patients in agonist maintenance treatment in those countries. Even in Switzerland, which has 23 HAT clinics (2 of them within prisons), the percentage is only 9%.

In countries belonging to the European Union, the extent of HAT is still modest (Figure 1) An estimated total of ca. 700,000 heroin addicts receive some kind of agonist maintenance treatment; this covers more than 50% of people with opioid depend-

Table. 1 Total capacity of HAT

Country	Nr of HAT clinics	Total capacity	Nr patients in AOT	% HAT of all AOT
Canada	2	140	14,700 (BC only)	0.9
Denmark	5	300	7,600	0.02
England	3	100	147,640	0.007
Germany	7	300	77,300	0.7
Netherlands	18	745	8,185 (MMT only)	(9.0)
Spain	1	56	69,111	0.001
Switzerland	23	1‘600	18,000	9.0
Belgium	(1)	?	17,482	?
Total	58	3‘095	Ca. 360‘018	Ca. 0.86

Sources: [28], European Drug Report 2015, personal communications (2013 data); AOT=Agonist Opioid Treatment

ence. The agonist medications are methadone (69%), buprenorphine (28%) and morphine/heroin (3%). Agonist maintenance treatment for prison inmates is available in 26 of the 30 countries monitored by the European Monitoring Centre for Drugs and Drug Abuse (EMCDDA); none of these is providing HAT to opioid-dependent prison inmates [7].

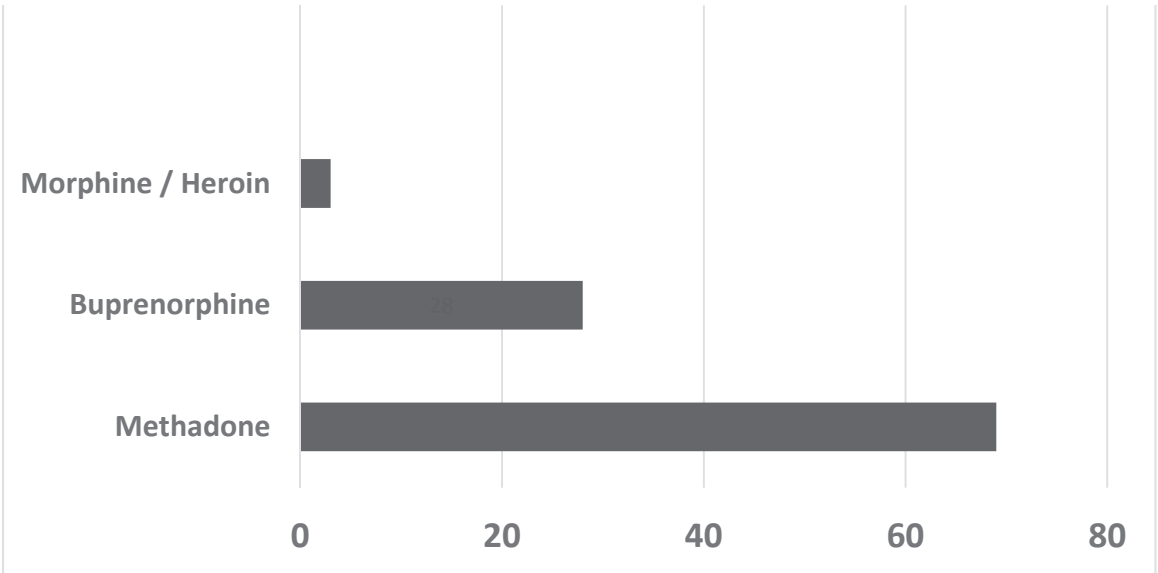
The relatively low numbers of opioid addicts receiving HAT is partly due to restrictive entry criteria: the target group is defined as treatment-refractory (other treatments must have failed repeatedly), and as suffering from major health and/or social deficits. But this target group is more numerous than the patients enrolled in HAT. How can this be explained?

In spite of the encouraging outcomes, concerns about and opposition to HAT were and remain considerable. It is worth looking at these concerns in the light of empirical outcome data.

6. The range of concerns against heroin-assisted treatment

The range of concerns covers therapeutic, economic and safety aspects, as well as negative consequences for prevention and other treatments:

- «Limitless hunger»: the demand for increasing dosages;
- «Hooked forever»: indicating the weakening of the will to recover;
- Increase of heroin-related mortality and



Source: European Drug Report 2015 (2013 data)

Figure 1. Capacity of HAT in the European Union

morbidity;
- Deviation of prescribed heroin to the illegal market;
- Lower threshold for starting heroin use, seen as sending the «wrong message»;
- Negative impact on other treatment approaches;
- Waste of financial and human resources.

6.1. Therapeutic concerns in the light of facts

The main therapeutic concerns are clearly not justified when confronted with outcome data from the Swiss national cohort study. The average daily dosages increased slightly during the induction phase, due to a careful testing of the individually appropriate dose; this was followed by a stabilization over about 4 months and a decrease after 8 months in treatment [24]. Also, when considering the various regimes of medications (i.v. heroin only, combined with heroin that is smoked or oral methadone), the mean dose for injectable heroin decreased significantly over time [11].

The treatment retention curve shows a continued decrease over 6 years; after about 3 years, half of the patients had left the programme [24].

Conclusion 1: therapeutic concerns about ever-increasing dosages and permanent retention are not confirmed by outcome data.

6.2. Concerns and facts about medical safety

Concerns about medical safety were further contradicted by outcome data from the Swiss cohort study. Mortality was definitely less than that in heroin addicts out of treatment, as also when compared heroin addicts in methadone treatment. Not a single case of death from prescribed heroin alone occurred, while there were a few cases of death due to mixed intoxication and overdose [25]. Infectious diseases related to intravenous injecting decreased; pre-existing infections received adequate treatment, and new infections were extremely rare, due to the reduction in illegal injections [29, 33].

Treatment outcomes with regard to health status and social integration in the Swiss cohort study show significant improvements in general and mental health status, in nutritional status (body mass index) and in injection-related skin disease [24]. Pregnancy and childbirth while being enrolled in HAT were repeatedly documented and did not present problems. One spontaneous abortion occurred when a patient started to withdraw from heroin. No malformation in the chidren was seen, and there was no case of sudden infant death [10].

Of those who left the programme, a substantial proportion went to follow-up treatments. According to the 3-year-follow up data, 37% changed to methadone or buprenorphine maintenance and 22% to drug-free treatment, while 15% dropped out of the programme. The other cases of dropout were due to hospitalization, imprisonment or death [24]. At 6-year follow up, patients who had left the programme showed a continued significant reduction of illicit substance use and criminal behaviour compared with entry data, as well as patients still in treatment [12].

Side-effects of HAT were systematically recorded in the Swiss cohort study and reported to a safety monitoring/group of experts. Histamin-like skin reactions, dizziness, respiratory difficulties, myoclonus, sedation – mostly mild and transient – were recorded; even in the few exceptional cases that occurred, they only led to a discontinuation of treatment [14]. In a few other cases, epileptic seizures occurred and were thoroughly investigated; in some cases, pre-existing epilepsy was documented [15]. A transient cerebral hypoxemy may cause seizure but can be prevented if patients do not lie down, but, rather, walk around for a while after injection.

Conclusion 2: HAT outcomes include a range of positive effects on somatic and psychiatric conditions, and reduce mortality and infection rates, but any side-effects of injected heroin must be taken care of through staff training and clinical practice.

6.3. Concerns about misuse of prescribed heroin

The removal of prepared heroin dosages that are then given to other addicts or sold on the black market is prevented through strict direct observation of injections by staff in the clinics, and clinics have to store heroin in safes to prevent stealing. Police staff have not reported any diversion of heroin from clinics.

Conclusion 3: no reports are available on the diversion of prescribed heroin to illicit use.

6.4. Concerns about public safety

Patients enrolled in HAT show a rapid and persistent significant decrease in criminal involvement and in small-scale drug trafficking [17]. In addition, typical drug-related delinquency in Swiss cities has declined significantly [17]. An increase in traffic accidents was prevented by the rule that patients had

to deposit their driving license during enrollment in HAT.

Conclusion 4: HAT results in an improvement of public safety.

6.5. *Concerns about negative impact on other treatment approaches*

A decline of applications for drug-free and methadone-assisted treatments was unlikely, due to the restrictive rule excluding all heroin addicts from the programme who had not repeatedly tried other treatments before. As a result, entries to drug-free treatment in Switzerland remained stable after the initiation of HAT, and entries to methadone-assisted treatment increased (Table 2). Also, the introduction of HAT contributed to an increased awareness of quality in addiction treatment, and drug-free residential treatment. In addition, methadone maintenance treatment benefited from the referral of non-compliant patients with continued illicit heroin use to HAT [31].

Data from the randomized controlled studies showed no preference given to heroin addicts over conventional treatments [29].

Conclusion 5: HAT does not undermine other approaches to the treatment of opioid dependence.

6.6. *Prevention concerns*

Did prescribing heroin as a medicine send the 'wrong message' to young people, inviting more experimentation with the substance? As a matter of fact, the incidence of new heroin users fell dramatically, to values recorded in the early 1970s before the heroin epidemic got out of control [21].

In discos, clubs, at raves, a vast range of drugs is available and consumed, but heroin is hardly ever on the list.

Conclusion 6: HAT has not lowered the threshold for starting heroin use; instead, its image became unattractive.

6.7. *Economic concerns*

HAT is more expensive than methadone-assisted treatment, due to the need to run the clinics involved all year long, including weekends and holidays. Are the expenses justified in the light of economic gains? Data from cost-benefit studies are available to answer the question.

Under experimental conditions, the economic evaluation of the German and the Dutch trials documented a great many benefits. The Dutch study found cost-effectiveness for the specific target group recruited to the trials [5]. Economic evaluation of the German trials came to the same conclusion of cost-effectiveness for experimental and control groups, and higher benefits for the experimental group [36]. Cost-effectiveness is also confirmed for the Canadian trial [22], and better cost-effectiveness in the experimental group for the RIOTT trial in England [3]. In addition, the Swiss prospective cohort study documented two-fold benefits compared with costs for HAT [13]. In all these studies, reduced health costs and law enforcement costs since entering HAT made primary contributions to the benefits.

Conclusion 7: although more expensive than oral maintenance treatments, HAT has proven its cost-effectiveness, and its superiority over control groups in randomized trials, so demonstrating that it is a good investment.

6.8. *Continued concerns expressed against wider use of HAT*

In spite of all this evidence, caution about extending HAT continues. How can this be understood? A detailed review identified the concerns as follows [28] about the adequacy of the scientific evidence

- Concerns about security, public safety, and potential for diversion and abuse
- Concern about rebound damage to other treatments, such as oral MMT and rehabilitation;
- Financial costs;

Table 2. Evolution of the Swiss treatment system since starting HAT

	1996	2000	2004	2008	2014
Drug-free residential	1,250*	1,3390	1,175	1,091	981
Methadone maintenance	12,000*	18,393	15,300	18,052	17,008
HAT	1,000*	1,240	1,515	1,449	1,656

Source: ISGF

- Hijacking by campaigning groups;
- Diamorphophobia;
- Safety.

While four of these concerns are dealt with above and their arguments are further invalidated by findings from the RCT studies, three new concerns appear here. The adequacy of scientific evidence is supported by the methodology used in the trials and by the data on sustained benefits; questions remaining open are mentioned and more research is now needed to improve understanding of the remission processes, the quality of life and social functioning of these patients.

A misinterpretation of the trials as being the first steps towards legalization must be prevented by clear and unambiguous information that will discourage such misinterpretation. Lastly, the prevailing image of heroin as a substance that is rightfully prohibited has replaced all the experience gained with the substance as a powerful medicine, especially in analgesia, after it has been used, in particular, in the UK for over a century.

As in the Swiss study, in all randomized controlled trials the advent of notable side-effects (mostly respiratory depression, at a rate of about 1 per 6,000 injections) was significantly more frequent in the experimental groups than in the control groups, therfore requiring adequate clinical observation and intervention skills [9, 28]. It may be added here that non-injectable preparations – whether smoked, intranasal or oral (either through immediate or slow release) – were introduced for patients who presented problems with injecting, or who preferred alternative routes of application; so far, severe events have not been documented.

The overall conclusion of the authors is clear; "This intensive intervention is for a patient population previously considered unresponsive to treatment. Inclusion of this low-volume, high-intensity treatment can now improve the impact of comprehensive healthcare provision" [29].

There is not much to add. Integrating HAT as part of a comprehensive system for the treatment of opioid dependence is in the interest of public health and public order, besides being in the interest of otherwise treatment-resistent heroin addicts.

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